

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
28 October 2004 (28.10.2004)

PCT

(10) International Publication Number
WO 2004/092146 A3

(51) International Patent Classification⁷: **A61K 31/426**,
31/415, 31/4406, C07D 277/46, 231/12, 213/55, C07C
311/21, A61P 3/10

(21) International Application Number:
PCT/US2004/011650

(22) International Filing Date: 14 April 2004 (14.04.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/463, 102 14 April 2003 (14.04.2003) US

(71) Applicant (for all designated States except US): **THE
INSTITUTES FOR PHARMACEUTICAL DISCOV-
ERY, LLC** [US/US]; 23 Business Park Drive, Branford,
CT 06405 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **VAN ZANDT,
Michael, C.** [US/US]; 91 Golden Hill Drive, Guilford,
CT 06437 (US). **FANG, Haiquan** [US/US]; 304 County
Road, Madison, CT 06443 (US). **HU, Shaojing** [US/US];
900 Mix Avenue, Unit 121, Hamden, CT 06514 (US).
WHITEHOUSE, Darren [US/US]; 40 Fishing Brook
Road, Westbrook, CT 06498 (US).

(74) Agent: **CRAWFORD, Bradley, W.**; McDonnell Boehnen
Hulbert & Berghoff, 300 South Wacker Drive, Chicago, IL
60606 (US).

(81) Designated States (unless otherwise indicated, for every
kind of national protection available): AE, AG, AL, AM,
AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,
GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE,
KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD,
MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG,
PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM,
ZW.

(84) Designated States (unless otherwise indicated, for every
kind of regional protection available): ARIPO (BW, GH,
GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW),
Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), Euro-
pean (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR,
GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK,
TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW,
ML, MR, NE, SN, TD, TG).

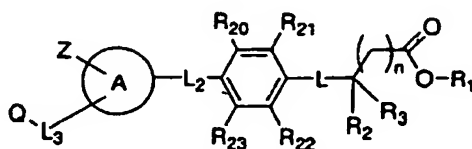
Published:

- with international search report
- before the expiration of the time limit for amending the
claims and to be republished in the event of receipt of
amendments

(88) Date of publication of the international search report:
29 December 2004

For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

(54) Title: **N-((((1,3-THIAZOL-2-YL) AMINO) CARBONYL) PHENYL) SULFONYL) PHENYLALANINE DERIVATIVES
AND RELATED COMPOUNDS FOR THE TREATMENT OF DIABETES**



(I)

(57) Abstract: The present
invention relates to compounds and
pharmaceutically acceptable salts
of formula (I), which are useful in
the treatment of metabolic disorders
related to insulin resistance or
hyperglycemia. These compounds

include inhibitors of protein tyrosine phosphatase (PTP-1B) that are useful in the treatment of diabetes and other PTP-1B mediated
diseases, such as cancer, neurodegenerative diseases and the like. The compounds of the invention are also useful in pharmaceutical
compositions and methods of treating the aforementioned conditions.

INTERNATIONAL SEARCH REPORT

International Application No.
PCT/US2004/011650

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K31/426 A61K31/415 A61K31/4406 C07D277/46 C07D231/12
C07D213/55 C07C311/21 A61P3/10

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K C07D C07C A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, BEILSTEIN Data, BIOSIS, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2002/077347 A1 (ABBOTT LABORATORIES (US)) 20 June 2002 (2002-06-20) page 1, paragraph 2; claims; examples	1, 20, 21
X	WO 02/08188 A (MERCK & CO INC (US)) 31 January 2002 (2002-01-31) page 1, paragraph 1; claims; examples	1, 20, 21
X	WO 02/064094 A (MERCK & CO INC (US)) 22 August 2002 (2002-08-22) page 1, paragraph 1 page 127; example 33 claim 1	1, 20, 21
	----- -/--	

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *Z* document member of the same patent family

Date of the actual completion of the international search

1 October 2004

Date of mailing of the international search report

15/10/2004

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax (+31-70) 340-3016

Authorized officer

Cortés, J

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US2004/011650

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 1 288 199 A (SHIONOGI & CO (JP)) 5 March 2003 (2003-03-05) page 8, line 46 pages 20-23; examples 60-76; tables 10-15 claims 1-11 -----	1,20,21
X	WO 02/28844 A (SHIONOGI & CO (JP)) 11 April 2002 (2002-04-11) pages 27-49; tables 1-19; compounds claims page 21, line 20 & WPI-abstract, AN: 2002-394341 '42! abstract -----	1,20,21
X	WO 01/83464 A (SHIONOGI & CO (JP)) 8 November 2001 (2001-11-08) pages 23-38; tables 1-16; compounds claims & WPI-abstract, AN: 2002-026249 '03! abstract -----	1,20,21
X	WO 01/83461 A (SHIONOGI & CO (JP)) 8 November 2001 (2001-11-08) pages 30-47; tables 1-8; compounds claims & WPI-abstract, AN: 2002-066512 '09! abstract -----	1,20,21
X	EP 0 950 656 A (SHIONOGI & CO (JP)) 20 October 1999 (1999-10-20) page 17, line 11, paragraph 69 pages 20-77; examples; tables 1-46 claims 1-23 -----	1,20,21
X	WO 99/32466 A (NOVARTIS (CH)) 1 July 1999 (1999-07-01) page 13, paragraph 2 pages 25-27; examples 11,13,20,23; table 1 claims -----	1,20,21
X	WO 97/38986 A (SEARLE & CO (US)) 23 October 1997 (1997-10-23) page 5, line 12 examples 50-53,62,63,67,72,79,80 claims -----	1,20,21
A	WO 99/58514 A (AMERICAN HOME PRODUCT (US)) 18 November 1999 (1999-11-18) pages 6-8 -----	1,20,21
P,X	DE 101 50 172 A (MORPHOCHEM AG) 30 April 2003 (2003-04-30) page 1, paragraph 1; claims; examples -----	1,20,21
	----- -/--	

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US2004/011650

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	WO 03/048140 A (JAPAN TOBACCO INC (JP)) 12 June 2003 (2003-06-12) page 1, paragraph 1 examples 50,51,53-55,57 claims -----	1,20,21
P,X	WO 2004/020409 A (MERCK & CO INC (US)) 11 March 2004 (2004-03-11) page 1, paragraph 1 examples 1-5,16,17,23 table 2; compounds 1,4-16,22-29,37-47 table 3; compounds claims -----	1,20,21
P,X	WO 03/035610 A (SHIONOGI & CO (JP)) 1 May 2003 (2003-05-01) pages 55-72; tables 20-39; compounds -----	1,20,21
P,X	WO 2004/010992 A (MERCK & CO INC (US)) 5 February 2004 (2004-02-05) page 1, paragraph 1 claims; examples -----	1,20,21

INTERNATIONAL SEARCH REPORT

national application No.
PCT/US2004/011650

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claim 21 is directed to a method of treatment of the human body, the search has been carried out and based on the alleged effects of the compounds.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US2004/011650

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
US 2002077347	A1	20-06-2002	NONE	
WO 0208188	A	31-01-2002	AU 7705601 A CA 2415742 A1 EP 1305285 A1 JP 2004513076 T WO 0208188 A1 US 2002042441 A1	05-02-2002 31-01-2002 02-05-2003 30-04-2004 31-01-2002 11-04-2002
WO 02064094	A	22-08-2002	CA 2437118 A1 EP 1366012 A2 JP 2004521124 T WO 02064094 A2 US 2004092596 A1	22-08-2002 03-12-2003 15-07-2004 22-08-2002 13-05-2004
EP 1288199	A	05-03-2003	AU 4882101 A EP 1288199 A1 WO 0183431 A1 US 2003158155 A1	12-11-2001 05-03-2003 08-11-2001 21-08-2003
WO 0228844	A	11-04-2002	AU 9228501 A CA 2423885 A1 CN 1466580 T EP 1331224 A1 WO 0228844 A1 US 2004024029 A1	15-04-2002 27-03-2003 07-01-2004 30-07-2003 11-04-2002 05-02-2004
WO 0183464	A	08-11-2001	AU 4876501 A WO 0183464 A1	12-11-2001 08-11-2001
WO 0183461	A	08-11-2001	AU 4882001 A WO 0183461 A1	12-11-2001 08-11-2001
EP 0950656	A	20-10-1999	AU 715764 B2 AU 1319597 A BR 9707010 A EP 0950656 A1 HU 9903687 A2 NO 983376 A NZ 325939 A SK 98498 A3 US 6207698 B1 US 6150394 A US 2003139379 A1 US 6441021 B1 CA 2242416 A1 CN 1214041 A CZ 9802252 A3 WO 9727174 A1 JP 2001316254 A PL 328270 A1 RU 2198656 C2 TR 9801419 T2 TW 575547 B US 2003225043 A1 US 6235768 B1	10-02-2000 20-08-1997 20-07-1999 20-10-1999 28-03-2000 14-09-1998 23-06-2000 13-04-1999 27-03-2001 21-11-2000 24-07-2003 27-08-2002 31-07-1997 14-04-1999 16-12-1998 31-07-1997 13-11-2001 18-01-1999 20-02-2003 21-10-1998 11-02-2004 04-12-2003 22-05-2001
WO 9932466	A	01-07-1999	AU 2415299 A	12-07-1999

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PC/US2004/011650

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9932466	A	WO 9932466 A1	01-07-1999
		ZA 9811705 A	07-09-1999
WO 9738986	A	23-10-1997	
		AP 1009 A	21-09-2001
		AT 233743 T	15-03-2003
		AU 734275 B2	07-06-2001
		AU 2722797 A	07-11-1997
		BG 102916 A	31-08-1999
		BR 1100403 A3	25-07-2000
		BR 9708574 A	03-08-1999
		CA 2249009 A1	23-10-1997
		CN 1216043 A ,B	05-05-1999
		CZ 9802710 A3	13-01-1999
		DE 69719496 D1	10-04-2003
		DE 69719496 T2	08-04-2004
		DK 892791 T3	23-06-2003
		EA 3319 B1	24-04-2003
		EE 9800351 A	15-04-1999
		EP 1288206 A1	05-03-2003
		EP 0892791 A1	27-01-1999
		ES 2194195 T3	16-11-2003
		HK 1019741 A1	02-05-2003
		HU 9901807 A2	28-09-1999
		IL 125849 A	31-10-2003
		JP 3382624 B2	04-03-2003
		JP 2000509029 T	18-07-2000
		JP 2003160554 A	03-06-2003
		KR 2000005395 A	25-01-2000
		LT 98142 A ,B	26-07-1999
		LV 12239 A ,B	20-03-1999
		NO 984727 A	14-12-1998
		NZ 331542 A	29-07-1999
		OA 11015 A	12-03-2003
		PL 329276 A1	15-03-1999
		PT 892791 T	30-06-2003
		SI 9720035 A	30-06-1999
		SK 124298 A3	13-04-1999
		TR 9802049 T2	18-01-1999
		US 5932598 A	03-08-1999
		WO 9738986 A1	23-10-1997
		US 6436967 B1	20-08-2002
		ZA 9703146 A	14-04-1998
WO 9958514	A	18-11-1999	
		AU 3791899 A	29-11-1999
		CA 2330558 A1	18-11-1999
		CN 1308619 T	15-08-2001
		EP 1077960 A1	28-02-2001
		JP 2002514633 T	21-05-2002
		WO 9958514 A1	18-11-1999
DE 10150172	A	30-04-2003	
		DE 10150172 A1	30-04-2003
WO 03048140	A	12-06-2003	
		CA 2469228 A1	12-06-2003
		EP 1452530 A1	01-09-2004
		WO 03048140 A1	12-06-2003
		JP 2003231679 A	19-08-2003
WO 2004020409	A	11-03-2004	
		WO 2004020408 A1	11-03-2004

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US2004/011650

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2004020409 A		WO 2004020409 A1	11-03-2004
WO 03035610 A	01-05-2003	WO 03035610 A1	01-05-2003
WO 2004010992 A	05-02-2004	WO 2004010992 A1	05-02-2004